

REMARKS

The present amendment is submitted in an earnest effort to advance the case to issue without delay.

Claims 8-9 and 12-13 were rejected under 35 U.S.C. § 112, second paragraph. The phrase "wherein the malonic acid is present in an amount ..." was identified as vague and indefinite for failing to indicate whether the subject referred to the acid salt or the acid itself. Applicant intended these claims to refer to the salt. These claims have been amended to clarify any indefiniteness which may have been present.

Claims 1 and 3-16 were rejected under 35 U.S.C. § 103(a) as unpatentable over Jokura et al. (U.S. Patent 5,641,495). Applicant traverses this rejection.

Applicant has found that skin softness, suppleness and flexibility can be improved through use of malonate salts. These salts are a combination of mono- and di-neutralized acid groups of malonic acid.

Jokura has but a single reference to malonic acid. See column 3 lines 33-34. Malonic is in a list with succinic, fumaric, maleic, glutaric, adipic, phthalic and terephthalic acids. Yet even here the reference mishandles the structure. The "X" of malonic is " CH_2 " instead of the specified " CH_3 ". The reference is silent as to malonic in all other respects.

Further, none of the Examples utilize malonic acid. The only exemplified dicarboxylic acid is succinic. Even the exemplification of succinic acid does not disclose the half neutralized acid salt, i.e. sodium or potassium hydrogen succinate.

The Jokura et al. Examples obscure and they even teach away from the half neutralized salt. For instance, Table 1 recites succinic acid and potassium succinate trihydrate. Nowhere is there mention of potassium hydrogen succinate trihydrate. Similarly in Table 2 succinic acid and sodium succinate are listed. Absent is sodium hydrogen succinate, the half salt.

Experiments have been performed via a Porcine Skin Test described in Example 9. Under Table VIII, it is seen that malonate salts are much better than glycolate or succinate salts with respect to improving skin flexibility (softness and suppleness). These results were surprising. Glycolates which are alpha-hydroxycarboxylic acids are well known to improve the flexibility of skin. Non-hydroxycarboxylic acids such as malonic have not received very much attention and are not particularly known for having any special skin activity. It was surprising to observe that the malonate was substantially better than the glycolate salt. Even more interesting was that succinate (malonic acid with one extra methylene group) did not perform well. Anyone skilled in the art would neither have expected nor selected malonates over succinates in considering the Jokura reference.

Jokura et al. discloses the unneutralized acid (component B) and the partially neutralized acid (component C). The free acid can only co-exist with a partially neutralized salt because of pKa considerations. There is thus no disclosure of a fully neutralized malonic acid (i.e. formula II at page 6).

The Examiner has highlighted the reference as teaching a molar ratio of dicarboxylic acid to dicarboxylic salt as being from 1:9 to 9:1. Jokura et al. states a ratio of free acid to neutralized acid. By contrast, applicant claims a ratio of mono to di-neutralized (i.e. half to fully neutralized) malonic acid. The ratio does not involve free acid.

Addition of a neutralizing agent to the free malonic acid would achieve mixtures of free and mono-salts (half neutralized). There would be no di-salt (fully neutralized) malonate present in a system that also included totally non-neutralized ("free") malonic acid. All three species, i.e. free, mono-salt (half neutralized) and di-salt (fully neutralized), could not coexist together. Yet the reference requires the presence of free acid, component B. Since the free acid must be present, the fully neutralized salt of that free acid could not coexist therewith. The pKa of malonic acid would not permit the presence of all three species. Thus, there is a fundamental inconsistency in Jokura et al. If the skilled chemist accepts the necessity for a free acid, then the di-salt of malonic acid could not be present. Jokura et al. lacks the claimed di-salt of formula II.

The Examiner has suggested that those of ordinary skill in the art could manipulate the acid to salt ratio through adjustment of pH. The motivation to manipulate the ratio was said by the Examiner to reside with desirability of adjusting pH between the disclosed 3 to 10 range. The pH range was noted at column 3, lines 30-

65. Further, motivation to partially or fully neutralize the acid was said to focus on avoiding irritation of the skin from the acidic form of malonic acid.

The fallacy of the foregoing argument is that the reference itself requires the presence of a very substantial amount of malonic in acid form, i.e. component (B). With the required full presence of dicarboxylic acid form, the skilled chemist reading this reference would not be motivated to neutralize to any extent that does not involve the presence of acid form. Yet the acid presence because of relative pKa requires the absence of the di-salt. Before any di-salt forms, all of the original dicarboxylic (malonic) acid must have at least one carboxy unit neutralized (i.e. a mono-salt). The di-salt cannot exist in the presence of totally unneutralized acid. Hence there can be no motivation to the skilled chemist to achieve a mixed mono- and di-salt. This chemist would know that free acid according to Jokura must be present and such cannot occur with any di-salt in the formula.

Applicant sees no disclosure of a half neutralized dicarboxylic acid salt. The Jokura et al. Examples obscure and may even teach away from the half neutralized salt. For instance, Table 1 recites succinic acid and potassium succinate trihydrate. Nowhere is there mention of potassium hydrogen succinate trihydrate. Similarly in Table 2, succinic acid and sodium succinate are listed. Absent is sodium hydrogen succinate, the half salt.

The Examiner has criticized applicant's comparative examples. Primarily the criticism is to lack of scope, especially with respect to comparisons against succinic acid/salts.

Applicant submits that the reference exemplifies the succinate next higher homolog of malonate. And except for a single instance in the broad specification, Jokura et al. does not discuss malonate. There is no example of a malonate. Since the disclosure is anemic on malonate yet expansive on succinate, applicant submits that the scope of the present showing is commensurate with the relative disclosures (succinate vs. malonate) in Jokura et al. The skilled chemist in reading Jokura et al. would be led to utilize or at least test succinate. Malonates would certainly not be an initial choice. Upon testing the succinate, the skilled chemist would be dissuaded from trying the malonate upon finding a relatively poor performance in a skin evaluation such as the claimed Porcine Skin Test. In certain ways Jokura et al. could be said to lead the skilled chemist away from using malonate by highlighting inferior performing dicarboxylic acids or salts.

Based on the foregoing considerations, it is evident that Jokura et al. does not present a *prima facie* case of obviousness. The simultaneous presence of both mono- and di- malonate salt is not present in the reference. Even were the claims to be considered *prima facie* obvious, the skilled chemist would not have been motivated to arrive at the present claims based on applicant's comments *vide supra*.

Claims 1, 3-4, 6-9, 11-13 and 15 were rejected under 35 U.S.C. § 103(a) as unpatentable over Beerse et al. (WO 00/61107). Applicant traverses this rejection.

Beerse et al. was cited specifically for the Example 14 disclosure. Therein is reported a composition comprising 3.20% sodium malonate and 4.00% malonic acid..

Unlike the claimed invention, Beerse does not disclose a half neutralized salt of malonic acid. There is reference to only one malonate salt mentioned. It is not known whether the "sodium malonate" is meant to be disodium malonate (fully neutralized) or sodium hydrogen malonate (half neutralized) variant.

Malonic acid is present as a proton donating agent. This means it is selected simply because it is an acid rather than for any special aspect of the organic radical. Indeed, mineral acids are considered by Beerse as the equivalent of any organic acid. Even giving the "proton donating agent" the broadest possible interpretation, the only remotely implied function is that of an anti-microbial substance. Thus, those skilled in the art would not be led to utilize malonates for the presently claimed purpose of controlling signs of aging such as improving skin softness, suppleness and flexibility. Present method claim 6 specifically focuses upon controlling the signs of aging through use of certain malonate salt combinations. Composition claim 1 inherently recites functionality of controlling signs of aging through requirement of a Flexibility Value greater than 1 in the Porcine Skin Test.

Beerse et al. requires a proton donating agent which at least in part must have unneutralized acid functionality, e.g. malonic acid. A mono-salt (half neutralized) of malonic can coexist with the di-acid form (unneutralized). What is not possible is that all three species, free acid, mono-salt (half neutralized) and di-salt (fully neutralized), would coexist together. The presence of mono- and di- salts would exclude equilibrium with free acid. Since the reference requires free acid, this reference cannot be teaching applicant's claim combination of half and fully neutralized malonate salt. The "sodium malonate" in Example 14 clearly must be the half neutralized sodium salt of malonic acid.

Selection of malonate salt mixtures for purposes of controlling the signs of aging is an unobvious selection. This is particularly so in contrast to the next closest homolog, i.e. succinate salts. Beerse et al. in Example 2 and 5 disclose a succinic acid/sodium succinate combination. Applicant has demonstrated in the specification under Example 9 that the malonate salt mixture gave a substantially better Flexibility Value in the Porcine Skin Test, compare 1.36 to 0.85 on Flexibility Value.

In response to applicant's arguments on function, the Examiner emphasized that Beerse teaches a combination comprising sodium malonate. From this, it is concluded that even though another advantage may have been recognized for sodium malonate, the different advantage or purpose is irrelevant. Apparently this is an inherency argument.

Applicant submits that the "sodium malonate" of the reference is not a combination of sodium malonate and sodium hydrogen malonate, i.e. di-salt and mono-salt, required by the present claims. Therefore, there is nothing inherent derived from the "sodium malonate"; it is not the same composition of salts presently claimed. The different function does here matter.

Another argument of the Examiner is that the skilled chemist would have been motivated to manipulate pH in the Beerse et al. formulas. By manipulation of pH, it is argued that the skilled chemist would have arrived at the claimed combination of half and fully neutralized salts.

J6829(C)
03-0022-CP/TR

Again the problem with this thesis is that Beerse et al. requires the presence of a certain amount of free acid. Any motivation to manipulate pH would be inhibited to achieve an equilibrium that would not include free acid. Yet the required presence of free acid eliminates the possibility of a di-salt.

In view of the foregoing amendment and comments, applicant requests the Examiner to reconsider the rejection and now allow the claims.

Respectfully submitted,

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